PTO/SB/68 (04-01)
Approved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

REQUEST FOR ACCESS TO AN APPLICATION UNDER 37 CFR 1.14(e)	
In re Application of	
Application Number Filed Nov. 1, 1995  Art Unit Examiner	
Ladiffile	
Paper No	
Assistant Commissioner for Patents Washington, DC 20231	
1. I hereby request access under 37 CFR 1.14(e)(2) to the application file record of the above-identified ABANDONED Application, which is not within the file jacket of a pending Continued Prosecution Application (CPA) (37 CFR 1.53(d)) and is: (CHECK ONE)	
(A) referred to in:	
United States Patent Application Publication No, page, line, United States Patent Number 6, 284, 236, column 63 _, line, or	
United States Patent Number 6, 284, 236, column 63, line, or	
an International Application which was filed on or after November 29, 2000 and which	
designates the United States, WIPO Pub. No, page, line	
☐ (B) referred to in an application that is open to public inspection as set forth in 37 CFR 1.11(b) or	
1.14(e)(2)(i), i.e., Application No, paper No, page, line	
2. I hereby request access under 37 CFR 1.14(e)(1) to an application in which the applicant has filed an authorization to lay open the complete application to the public.	
Chors Riky 3/12/02	
Signature	
Chois Riley FORPTOUSE ONLY	
Typed or printed name Approved by:	
(initials) Unit:	

Burden Hour Statement: This form is estimated to take 0.2 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.



# (12) United States Patent Wiley et al.

(10) Patent No.:

US 6,284,236 B1

(45) Date of Patent:

Sep. 4, 2001

# (54) CYTOKINE THAT INDUCES APOPTOSIS

Inventors: Steven R. Wiley; Raymond G. Goodwin, both of Seattle, WA (US)

Assignee: Immunex Corporation, Seattle, WA (US)

Notice:

(\*)

Subject to any disclaimer, the term of this

patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

Appl. No.: 09/320,424 (21)

(22) Filed: May 26, 1999

#### Related U.S. Application Data

- Continuation-in-part of application No. 09/190,046, filed on Nov. 10, 1998, now abandoned, which is a continuation-in-part of application No. 09/048,641, filed on Mar. 26, 1998, now abandoned, which is a continuation-in-part of application No. 08/670,354, filed on Jun. 25, 1996, now Pat. No. 5,763,223, which is a continuation-in-part of application No. 08/548,368, filed on Nov. 1, 1995, now abandoned which is a continuation-in-part of application No. 08/496,632, filed on Jun. 29, 1995, now abandoned.
- Int. Cl.<sup>7</sup> ...... A61K 38/19; C07K 14/52; C12N 5/10; C12N 15/19; C12N 15/63
- (52)514/12; 530/351; 435/69.5; 435/320.1; 435/325; 435/471; 435/71.1; 435/71.2; 435/252.3; 536/23.1; 536/23.5
- Field of Search ...... 530/350, 351; (58)574/2, 8, 12; 435/69.5, 325, 252.3, 254.11, 471, 71.1, 71.2, 320.1; 536/23.1, 23.5; 424/85.1

#### (56)References Cited

#### U.S. PATENT DOCUMENTS

5,512,435	4/1996	Renschler et al 435/6
5,716,805	2/1998	Srinivasan et al 435/69.1
5,876,954	3/1999	Perron et al 435/23

## FOREIGN PATENT DOCUMENTS

`wo	97/25428	7/1997	(WO).
WO	97/33899	9/1997	(WO).
WO	97/46686	12/1997	(WO).
wo	99/07408	2/1999	(WO).
wo	99/36535	7/1999	(WO).
WO	99/48527	9/1999	(WO).

### OTHER PUBLICATIONS

Rieger et al. Glossary of Genetics & Cytogenetics, Fourth Edition, Springer-Verlag, pp. 16-19 1976.\*

Mikayama et al. Proc. Natl. Acad. Sci. USa vol. 90, pp. 10056-10060, 1993.\*

Voet et al. Biochemistry. John Wiley & Sons, Inc. pp. 126-128 and 228-234, 1976.\*

Hillier et al., NCBI databank record, accession No. T90422, Mar. 20, 1995.

Hillier et al., NCBI databank record, accession No. T82085, Mar. 10, 1995.

Bell, G.I. and Takeda, J., NCBI databank record, accession No. T10524, Jul. 28, 1993.

Hillier et al., NCBI databank record, accession No. R31020, Apr. 28, 1995.

Genexpress, NCBI databank record, accession No. Z36726, Aug. 18, 1994.

Jo, M. et al., "Apoptosis induced in normal human hepatocytes by tumor necrosis factor-related apoptosis-inducing ligand," Nature Medicine 6: 564-567, May 2000.

Banner al., "Crystal structure of the soluble human 55 kd TNF receptor-human TNFBcomplex: implications for TNF receptor activation," Cell 73: 431-445, 1993.

Belliveau et al., "Presence of the cytokine APO-2L (TRAIL), in the cerebrospinal fluid of multiple sclerosis patients," Society for Neuroscience Abstracts 23(1-2). 1997; p. 2207.

Belliveau et al., "Presence of the cytokine, APO-2L (TRAIL), in the cerebrospinal fluid of multiple sclerosis patients," Poster presented at the 27th Annual Meeting of the Society for Neuroscience, Oct. 25-30, 1997, New Orleans. Beutler and van Huffel, "Unraveling function in the TNF ligand and receptor families," Science 264: 667-668, 1994. Bowie, et al., "Deciphering the message in protein sequences: tolerance to amino acid substitutions," Science 247: 1306-1310, 1990.

Goodwin et al., "Molecular cloning of a ligand for the inducible T Cell gene 4-1BB: a member of an emerging family of cytokines with homology to tumor necrosis factor," Eur. J. Immunol. 23: 2631-2641, 1993.

Goodwin et al., "Study of the structure and function of Trail, a new member of the TNF ligand family," Eur. Cytokine Network 7 (2): 166, 1996.

Hollenbaugh et al., "Construction of immunoglobulin fusion proteins," Current Protocols in Immunology, Supp. 4, 1992, 10.19.1-10.19.11.

Hoppe et al., "A parallel three stranded α-helical bundle at the nucleation site of collagen triple-helix formation," FEBS Letters 344: 191-195, 1994.

Kroemer, "The pharmacology of T cell apoptosis," Adv. Immunol. 58: 211-296, 1995.

Landschultz et al., "The Leucine zipper: a hypothetical structure common to a new class of DNA binding proteins," Science 240: 1759-1764, 1988.

Marsters et al., "Activation of apoptosis by Apo-2 ligand is independent of FADD but blocked by CrmA," Current Biology 6 (6): 750, 1996.

Menard et al., "A gliotoxic factor and multiple sclerosis," J Neurological Sciences 154: 209-221, 1998.

## (List continued on next page.)

Primary Examiner—Prema Mertz (74) Attorney, Agent, or Firm-Kathryn A. Anderson

#### (57) **ABSTRACT**

A novel cytokine designated TRAIL induces apoptosis of certain target cells, including cancer cells and virally infected cells. Isolated DNA sequences encoding TRAIL are disclosed, along with expression vectors and transformed host cells useful in producing TRAIL polypeptides. Antibodies that specifically bind TRAIL are provided as well.

# 59 Claims, 4 Drawing Sheets